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| 10/784,393 | 02/23/2004 | Aaron T. Timperman | 22085/2112 | 8432 |

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| EXAMINER | |
|---|---|
| BEISNER, WILLIAM H | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1744 | |

DATE MAILED: 06/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/784,393 | TIMPERMAN, AARON T. | |
| | Examiner | Art Unit | |
| | William H. Beisner | 1744 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *29 March 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,3 and 5-35* is/are pending in the application.

4a) Of the above claim(s) *13-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3 and 5-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Election/Restrictions*

1. Claims 13-35 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 10/8/04.

### *Claim Rejections - 35 USC § 103*

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

4. Claims 1, 3 and 5-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nelson et al.(US 6,007,690) in view of Wang et al.(Rapid Communications in Mass Spectrometry).

The reference of Nelson et al. discloses a microfluidic device that includes an inlet channel (66); a reaction channel (enrichment channel, 62) and solid supports (3) in communication with the reaction channel and capable of concentrating a charged analyte produced by a reaction in the reaction channel.

While the reference of Nelson et al. discloses that the reaction channel (enrichment channel, 62) may be used as a microreactor for protein digestion (See column 4, lines 43-67), the reference does not specifically discloses that enzyme is located in the channel.

The reference of Wang et al. clearly discloses that it is conventional in the art to provide enzyme within a reaction channel on a microfluidic device (See Figure1 and related disclosure).

In view of this teaching, it would have been obvious to one of ordinary skill in the art at the time the invention was made to provide the enrichment channel (62) of the reference of Nelson et al. with an enzyme for the known and expected result of providing an art recognized means for protein digestion so as to provide a microreactor as suggested by the reference of Nelson et al.

With respect to the specifics of the membrane employed of claims 1 and 3, the reference of Nelson et al. discloses a number of possible solid supports that can be employed with respect to the enrichment channel (See column 6, lines 1-56). Specifically, the reference of Nelson et al. discloses the use of "ion-exchange membranes" (See column 6, lines 37-45). An ion-exchange membrane is changed and can have pores that are larger than the charged analyte that it binds with since it is merely functioning as a support matrix for binding rather than a physical particle filter. As a result, in the absence of a showing of criticality and/or unexpected results, it would have been obvious to one of ordinary skill in the art at the time the invention was made to

determine the optimum material for enclosing the enrichment channel based merely on the specifics of the analyte to be reacted and/or detected in the system.

With respect to the charge on the membrane of claims 5-10, based merely on the specific material of the membrane employed, the material will inherently include a positive or negative charge. Additionally, it would have been obvious to one of ordinary skill in the art to provide a desired charge for the capture of reaction products as suggested by the reference of Nelson et al. (See column 6, lines 46-53).

With respect to the side channels of claims 6-10, the reference of Nelson et al. discloses the use of side channels (14, 15).

With respect to the electrodes of claims 9 and 10, the reference of Nelson et al. discloses the use of electrodes (60 and 61) with respect to the side channels. As is known in the field of electrophoresis, the voltage applied to the electrodes can be positive or negative based merely on the desired direction of flow. As a result, the electrodes of Nelson et al. are structurally capable of being positive or negative.

With respect to the claimed upstream module of claim 11, it would have been obvious to one of ordinary skill in the art to purify the sample prior to introduction into the microreactor system for the known and expected result of removing any components of the sample which may interfere with the analysis reactions and/or detection.

With respect to the downstream separation module of claim 12, the reference of Wang et al. discloses that it is conventional in the art to provide the protein digested sample of a microfluidic device to a MS for further separation and analysis (See Figure 1 and related text). As a result, it would have been obvious to one of ordinary skill in the art at the time the invention

was made to further analyze the reaction products of the device of Nelson et al. using a MS as suggested by the reference of Wang et al.

***Response to Arguments***

5. With respect to the rejection of claims 1-12 under 35 USC 103 over the combination of the references of Nelson et al. and Wang et al., Applicants advance the following arguments:

a) The instant claims now require "at least one membrane having a plurality of pores" "wherein the pores of the membrane have a pore diameter greater than a diameter of the charged analyte" and the references of Nelson and Wang do not teach or suggest concentrating a charged analyte with a membrane wherein the pores of the membrane are larger than the diameter of the analyte (See pages 8-9 of the response dated 3/29/05).

b) The instant invention allows a charged analyte to concentrate in front of a membrane wherein the pores of the membrane are larger than the diameter of the analyte and "claim 1 has been amended to require a device capable of concentrating analytes in front of a membrane wherein the pores of the membrane are larger than the diameter of the analyte" (See page 10 of the response dated 3/29/05).

c) The reference of Nelson merely discloses a microfluidic device having a membrane capable of blocking or binding a desired analyte. The reference of Nelson does not disclose or suggest the ability to concentrate a charged analyte in front of a membrane wherein the pore size of the membrane is larger than the diameter of the analyte (See pages 10-13 of the response dated 3/29/05).

d) The reference of Wang et al. fails to correct for the deficiencies with respect to the reference of Nelson et al. (See page 13 of the response dated 3/29/05).

e) The combination of the references of Nelson et al. and Wang et al. do not disclose, suggest or teach the device of claim 1.

6. Applicants' arguments above are not found to be persuasive for the following reasons:

In response to argument a) above, the Examiner is of the position that the reference of Nelson et al. suggests the use of a membrane capable of binding a desired analyte (See column 6, lines 30-45). The use of an ion-exchange membrane or binding membrane involves the binding of a charged analyte with the membrane. As a result, the membrane suggested by the reference of Nelson et al. would be a charged membrane. Furthermore, the when using a membrane as suggested by the reference of Nelson et al. in enrichment channel (70) of Figure 11, the membrane would be required to be porous wherein the pores have a diameter larger than the diameter of the analyte concentrated by the membrane. If not, the analyte would not be capable of passing through the membrane and on to the analysis section of the device as required by the disclosure of the reference of Nelson et al. (See pages 11-12 of Applicants response dated 3/29/05 with respect to the discussion of Figure 11 of the reference of Nelson et al.). As a result, the Examiner is of the position that the use of a binding membrane as suggested by the reference of Nelson et al. within section (70) of the device would meet the claimed structure of claim 1, "at least one membrane having a plurality of pores" "wherein the pores of the membrane have a pore diameter greater than a diameter of the charged analyte".

In response to arguments b) and c) above, while the reference of Nelson et al. is silent to the concentration of analyte in front of the membrane, the Examiner is of the position that the structure suggested by the combination of the references of Nelson et al. and Wang et al. meets the structure of instant claim 1. The membrane suggested by Nelson et al. would be capable of concentrating analyte in front of the membrane when the sample includes an analyte that has an opposite charge to that of the membrane positioned within the device. Note statements of intended use carry no patentable weight in apparatus type claims.

In response to argument d) above, the reference of Wang et al. was not relied upon to disclose the claimed porous membrane. Rather the reference was merely recited to address the additional claim limitation of an enzyme positioned within the microchannel device.

In response to argument e) above, for the reasons discussed above, the Examiner is of the position that the combination of the references of Nelson et al. and Wang et al. meet the claimed structure of claim 1.

***Conclusion***

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to William H. Beisner whose telephone number is 571-272-1269. The examiner can normally be reached on Tues. to Fri. and alt. Mon. from 6:15am to 3:45pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John Kim can be reached on 571-272-1142. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

William H. Beisner
Primary Examiner
Art Unit 1744

WHB